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The lesser of two evils: A qualitative study of quetiapine use by family physicians

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Abstract

Background:

Quetiapine is an antipsychotic, widely prescribed off-label by family physicians, despite evidence that safer alternatives exist. The aim of this research was to explore, in-depth, family physicians' reasons for this behavior.

Methods: Qualitative interviews with fifteen urban family physicians in Alberta, Canada. Participants were purposively selected based on gender, years of experience, and practice type. Interviews explored participants' experiences prescribing quetiapine. Interviews were recorded, transcribed verbatim, and coded using thematic analysis.

Results: A wish to support complex patients' day-to-day function without causing benzodiazepine addiction motivated participants to prescribe quetiapine. The indications were varied and included incomplete symptom resolution, unclear or multiple mental health diagnoses, and complicated psychosocial problems. Family physicians benchmarked their prescribing against peers and were reluctant to stop medication started by colleagues. Limited knowledge of quetiapine's side effects led prescribers to choose low doses.

Interpretation: Quetiapine helped family physicians treat patients with complex mental health problems without prescribing benzodiazepines, but awareness of adverse effects of quetiapine was poor. Education about quetiapine should combine psychopharmacology with multi-disciplinary educational initiatives, which focus on symptom resolution, co-morbidity and non-drug options to promote more appropriate prescribing.

Key words: family physicians, quetiapine, prescribing, qualitative research

Introduction

Quetiapine is the most widely prescribed antipsychotic in North America. In 2008, antipsychotic drugs became the top selling drug class in the US, with estimated sales of US$14.6 billion. [1] [2] Global antipsychotic sales in 2010, were US$25.4 billion; of these Seroquel™ (quetiapine) was the 5th biggest selling pharmaceutical worldwide, costing an estimated US$6.8 billion.[3] In Canada, prescriptions for quetiapine between 2005-2012 rose by 300%. Using the IMS Brogan Canadian CompuScript databases to identify prescribing data, researchers found that 50% of filled antipsychotic prescriptions in Canada were for quetiapine and most came from family physicians.[4] Although quetiapine is licensed for treatment of schizophrenia, bipolar disorder, and as an adjunctive to antidepressants in moderate to severe depression, much prescribing of quetiapine is off-label.[4, 5] Off-label prescribing of antipsychotics has been studied extensively, including a meta-analysis of one hundred and seventy studies.[6] Leslie et al, examined prescribing data from the Department of Veteran Affairs (US) and found that 60.2% of the 279,778 patients who received a prescription for an antipsychotic in 2007, had no indication for its licensed use.[7] Of these, 43% were prescribed quetiapine.[7] More recently, UK researchers examined prescribing data using The Health Improvement Network (THIN), a primary care database of almost 10 million patients. They found that only 36% (n=4824) of those prescribed quetiapine had a serious mental illness recorded.[5] Insomnia, anxiety and behavioral disturbance in elderly people and children, are common reasons for off-label use.[2, 8, 9] Evidence of benefit for these indications is disputed.[9-11] Metabolic, neurological, and cardiovascular side effects[10, 12] pose a significant risk of harm.[12, 13] Maglione et al, calculated a number needed to harm (NNH) of 8 for neurological adverse effects in patients with

dementia (OR 5.16, 95% CI 2.93-9.51), and an NNH of 16 (OR 2.72, 95% CI 2.07-3.56) for weight gain and increased appetite in other conditions.[6]

A number of professional bodies such at the Canadian Psychiatric Association[14], the American Psychiatric Association[15], the American Diabetes Association[16] and the American Geriatrics Association[17] caution physicians to use antipsychotics judiciously.[15, 17, 18] The Choosing Wisely campaign made four recommendations for restricting the use of second generation antipsychotics, in particular to avoid its use for insomnia (in any age-group) and behavioral disturbance, particularly in patients with Attention Deficit Hyperactivity Disorder and dementia. [19] A number of guidelines on de-prescribing of antipsychotics have recently been published.[20, 21]

Decisions to prescribe are not simply a matter of knowing the indications for drugs. These are influenced by characteristics of patients,[22] practitioners,[23, 24 25, 26] the organizational settings in which physicians work,[27, 28] commercial influences,[25, 29] and interactions between those various factors. Continuing professional development is a means of influencing prescribing behavior but this calls for a clear understanding of the complex web of factors that cause questionable behaviors to exist and persist. The exploratory nature of qualitative research is well suited to scratching below the surface of non-ideal behaviors and identifying obstacles and facilitators to the adoption of desired behaviors. We therefore set out to explore, in depth, why and how family physicians prescribed quetiapine.

Methods

This qualitative interview study was set in urban family practice in Alberta, Canada. The researchers were a female family physician (MK) interested in mental health, a female neurologist with an interest in pharmacoepidemiology and mental health (TP), and a male endocrinologist, working in medical education research (TD). All have experience of conducting qualitative research.

Sampling and Recruitment: Study information comprising an introductory email, cover letter, and informed consent, were disseminated via faculty email lists (Department of Family Medicine, University of Calgary). We contacted volunteers by telephone to give more information, answer questions, ensure anonymity, and arrange an interview. We informed participants that the study objective was explore family physician use of quetiapine and gain a better understanding of prescribing practices. No one who contacted the study team declined interview.

We constructed a sampling frame to obtain a purposive sample by gender, years of experience, and practice type. Using this enabled us to track participant characteristics to ensure we interviewed physicians with a range of experience. Initially an over representation of experienced physicians volunteered, so we stopped recruiting from that group, and focused on more recent graduates and physicians working in walk-in clinics. Sampling in the later stages was influenced by the findings of interim analysis.

Data collection: To minimize any social desirability bias that might result from group interaction and ensure physicians felt comfortable providing in-depth descriptions of their prescribing practices, we chose one-to-one interviews to collect data. MK or TP conducted interviews in person (13 interviews) or by telephone (2 interviews), for which they offered participants a CN$250 honorarium. Three participants were known to MK and one to TP, based on professional interactions. None were known in a personal capacity.

A semi-structured interview schedule was developed, and piloted. MK sent an initial version of the interview schedule to family doctors in her clinic (n=6) for feedback. She then conducted a pilot interview with two colleagues and amended the schedule. These interviews did not contribute to the final dataset. The interview opened by asking participants to describe their clinical practice and general approach to patients with mental health concerns. Participants then described their experiences of

prescribing quetiapine. We followed up issues they raised and asked additional questions about patterns of quetiapine use, resources, prescribing influences, and patient factors. The final interview schedule is available in Appendix A. Interviews were conducted between Oct 2015 and April 2016.

Analysis: Data collection and analysis were iterative and used to inform ongoing sampling and interview modification. Interviews were recorded, transcribed and coded, using template analysis. This is a flexible form of thematic analysis[30] in which an initial template was devised based on a priori codes developed from the literature. This was modified in response to open coding of transcripts. Transcripts were read independently, and initial codes identified. MK and TP met repeatedly to discuss and refine the preliminary template. We then applied the template to further data and refined it progressively until we had arrived at a final template, over the course of 8 meetings. To prevent the findings being unduly influenced by our individual preconceptions, we discussed our responses to the data and recorded field notes after each meeting to capture our different perspectives as generalist and specialist physician respectively. A senior physician, experienced in qualitative prescribing research (TD) promoted researcher reflexivity, through discussion and by challenging the interpretation, during the initial phase of analysis, mid-way, and at its final stage. Analysis continued until we reached data saturation, with no new themes emerging from latter interviews.

We gauged the trustworthiness of our findings by sending our final template and draft paper to all participants as a form of member checking. Four participants responded and agreed with the findings. In addition, we presented findings at three family medicine conferences (provincial, national and international).

Ethics: This study received approval from the Conjoint Health Research Ethics Board (CHREB), University of Calgary.

Results

Participants: Fifteen physicians (8 men, 7 women) participated (Table 1). Interviews lasted 29-66 minutes (average 40 minutes) and were conducted in locations determined by participants, which included their practices, homes, coffee shops, or the researchers' offices. Twelve participants worked as family physicians in the community and three were family physicians working part-time (1) or full-time (2) as hospitalists. Four participants worked in clinics designed to support patients with complex psychosocial needs such as chronic mental illness, low income, unemployment, and homelessness. These patients are referred to as 'complex patients' hereafter. Most participants worked in extended primary care teams, which included behavioral health consultants (13 interviewees), social workers (6 interviewees), and joint physician-psychologist appointments (3 interviewees).

Our final template, which details themes and subthemes that summarize participants' use of quetiapine, is shown in Appendix B. This narrative elaborates those themes. Further exemplar quotations are provided in Appendix C. Participants were torn between feeling responsible for relieving patients' symptoms so they could function in society, and giving them benzodiazepines to which they might become addicted. Quetiapine seemed to balance efficacy against safety (Figure 1).

Mental health plus – a solution for complex patients?

Participants did not see quetiapine as a first line treatment for depression, anxiety, behavioral disorders, or insomnia. They reserved it for patients unresponsive to first line therapies, patients with multiple psychiatric diagnoses, or patients with challenging psychological or social histories. Quetiapine was able to 'calm', 'take the edge off', or 'settle' agitated or distressed patients. One physician described this as '*mental health plus'*. The decision to use quetiapine was based on physicians' belief that it relieved

distressing symptoms and helped patients retain some semblance of normality – be it to remain in work, take care of their families, or keep their hostel bed (Table 2, quotation 1, 2, 3, 4).

Choosing cautiously – the lesser of two evils

Participants selected quetiapine because of its non-addictive nature and they felt it was less likely to be abused. They wanted to avoid benzodiazepines, so quetiapine was 'the lesser of two evils' (Male, full-time hospitalist, 5-9 years in practice) (see also Table 2, quotation 5, 6)

My patients are fine on low doses

Participants were unfamiliar with quetiapine's mechanism of action and knew variable amounts about its adverse effects. Most expressed belief that it was a reasonably safe option and were comfortable to prescribe it at a dose of 25 to 50 mg per day. Since they thought this was safe, they did not monitor patients for adverse effects (Table 2, quotation 7). Few participants informed patients that quetiapine was an antipsychotic and, if they did, couched it as 'not being used for that' and emphasized that the dose was low.

Prescribing influences

Other physicians, such as psychiatrists, colleagues in family medicine, and preceptors were the people who most often guided participants towards using quetiapine. Participants did not identify messaging from pharmaceutical companies or demand from patients as significant prescribing influences (Table 2, quotation 8, 9, 10).

Caring for patients on quetiapine initiated by another physician created dilemmas. Participants usually continued prescriptions initiated in hospital, particularly if started by a psychiatrist, although they did not always know who had started it, or why. When another family physician had started quetiapine, participants did not routinely re-evaluate its use before renewing the prescription. Some participants

said patients were reluctant to stop quetiapine and, since it had seemed to provide therapeutic benefit, chose to continue it (Table 2, quotation 10).

Discussion

Main results

Family physicians' quetiapine prescribing was much less paradoxical, at the level of the individual physician and patient, than evidence at an epidemiological level suggested. Physicians and patients were between a rock and a hard place: treatment resistant mental illness versus benzodiazepine addiction. Participants perceived low dose quetiapine as relatively safe, effective, and they were under the impression that fellow family physicians and psychiatrists thought the same. Widespread prescribing of quetiapine for off-label indications could too easily give the impression of indiscriminate use. Participants in this research felt they prescribed quetiapine carefully, taking account of patients' symptoms, and social situations. Their knowledge however, of the mechanism of action of quetiapine, its side-effects and the need for monitoring was poor. None of our participants had a system in place to monitor patients on quetiapine, compounded by their lack of knowledge as to what side-effects to look for. This knowledge gap contributed to the preferential use of quetiapine over other drugs, and likely a failure to recognize and properly attribute quetiapine induced adverse effects to the drug. Ongoing use of quetiapine was compounded by an assumption among hospitalists, family physicians and psychiatrists that patients were prescribed quetiapine for clear indications, but these were poorly communicated. Hospital doctors expected family doctors to know when to stop quetiapine yet the latter were reluctant to discontinue psychotropic medications for fear of causing mental distress or relapses. Patients were seldom informed that the medication they were prescribed was an antipsychotic.

These findings resonate with previous prescribing studies which indicate that physicians' prescribing decisions are strongly impacted by personal experience,[23, 25, 26] social influences and healthcare systems.[24, 31] The role of social factors influencing the implementation of Choosing Wisely

recommendations and in particular, prescribing recommendations, is supported in a recent survey of family physicians and primary care workers in the US.[22] Notably, the recommendations health care workers felt would be the most problematic related to caring for symptomatic patients, because of potential negative impact on the doctor-patient relationship. In our study, family physicians negotiated use of quetiapine –balancing immediate symptoms with other priorities.

A key benefit identified by our participants was the calming effect of quetiapine. Family physicians perceived quetiapine as a safe and effective alternative to potentially addictive medication.[1] Quetiapine appeared to fill the niche previously occupied by benzodiazepines. [32] Yet our participants' knowledge of the mechanism of action of quetiapine and safety concerns was limited – despite recent educational campaigns[15, 17]. Family physicians mitigated this gap, through use of low doses and, in keeping with previous literature on guideline use[33, 34], prioritized real world experience by colleagues, both peers and specialists over information. Ambivalent attitudes and perceptions have been identified as important determinants of inappropriate prescribing.[35] A recent initiative which incorporated behavior change techniques tailored to prescriber characteristics using e-learning showed increased adherence with guidelines, reduced prescribing and increased use of psychosocial interventions by family physician trainees.[36]

Strengths and limitations

One strength is use of qualitative methods to explore family physicians' experiences with quetiapine. This allowed family physicians to detail their use of quetiapine, which enabled us to investigate what they said they did, rather than their opinions of what they should do. Their frankness and willingness to admit ignorance gave us confidence in the validity of their accounts of their practices. Our

complementary perspectives of family physician and specialist helped us both understand and challenge each other during the analysis.

This is an exploratory study, our sample consisted of physicians from a single urban centre. We continued interviewing until our analysis achieved data saturation. Although four of our participants worked with vulnerable populations, all of our participants described quetiapine use for complex patients. Whilst our study design was in line with qualitative research practice, a more exhaustive sample size might have added extra insights. Finally, it is possible that participants may have felt some imperative to please us, as physician colleagues, in their responses.

Conclusion

This qualitative study provides insights into family physicians reasons for prescribing quetiapine. While quetiapine was not used first line for mental ill-health, it was commonly prescribed as an adjunct, particularly to sedate anxious patients, or those experiencing sleep difficulty. This practice was justified, in the eyes of participants, through use of low doses and that it was common practice by colleagues. However, participants were ill-informed on how quetiapine worked, its adverse effects and the need for ongoing monitoring. Our findings point to an urgent need for increased education about quetiapine. Such initiatives should focus on increasing knowledge and addressing the psychological dynamics of prescribing, such as attitudes, perceptions and self-efficacy, to promote safe prescribing. Further research is needed to understand, why, with resources in hand, physicians felt pressure to choose between the 'lesser of two evils', both of which were classes of drugs, when psychological therapies were available. Additional research to understand patient's perspectives on the use of quetiapine would be helpful to help guide physicians in their conversations with patients.

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Table 1: Characteristics of participants

Characteristic	N (%)
Sex	
Male	8 (53)
Female	7 (47)
Years in Practice	
< 5	1 (7)
5-9	4 (27)
10-14	4 (27)
>15	6 (40)
Practice type	
Community family practice (general)	6 (47)
Community family practice (vulnerable/inner city population)	4 (20)
Walk-in clinic	2 (13)
Family doctor working in hospital (hospitalist)	3 (20)
Access to extended mental health services in the community or hospital	
Yes	13
No	2

Table 2: Themes and illustrative quotations

Theme	Quotation no.	Illustrative quotation
Mental health plus	1	So most of us family docs are used to using zopiclone for sleep and so the reason I think, I think I'm seeing so much quetiapine is because there's another psychiatric aspect to what they're seeing, so it's not just sleep….There's either an anxiety component, an agitation component, there's something else. It's sleep plus. (Female part-time hospitalist, 5-9 years in practice)
	2	I would see patients who I guess were primarily coming out of jail and a lot of those patients would be on quetiapine for aggressive behavior, for sleep, for anxiety, and some of them would even say, some of those patients would say that it helped them sort of quell their addictions, so that's probably where I got exposed to it the most. (Male, full-time community practice, vulnerable populations, 5-9 years in practice)
	3	Mhm, so a patient comes in with, so middle-aged patient, either female or male coming in with predominantly generalized anxiety, some depressive features, some insomnia, who is suffering most acutely from the insomnia and the fatigue as a result which then ends up fueling the anxiety and depressive symptoms, so would then start at a low dose concurrently an antidepressant in addition to very low dose, say 12.5 mg, of quetiapine at night just to help with the sleep initiation. (Female, community practice, 5-9 years in practice)
	4	On the other hand, that's one complaint that I think we struggle with addressing because you just don't have a lot of options that actually are reliably effective and don't come with a host of other problems, so there's certainly been times where I think we've prescribed quetiapine just as a sleeping aid simply because we don't want to prescribe anything else and the encounter is not going to end, you know, we sort of have to give up a prescription for that in order to meet other goals, so some negotiation where sort of picking at a bit of a battle with the patient that might not be very therapeutic over that issue. There may be other things that we're working on as a priority. (Male, community, > 15 years in practice)
Choosing cautiously – the lesser of two evils	5	You need to stay away as much as possible from benzodiazepines or zopiclone or anything in that class because of the addictive properties and, well dependence really, and the interference with sleep architecture. Now admittedly, I don't fully understand how quetiapine either augments or disrupts sleep architecture so that I don't know. I don't know anything about the long-term effects but as a result of us needing to move away from benzos, etc., it seems like quetiapine has moved into that vacuum that was created. (Female community practice, vulnerable populations, 5-9 years in practice)

	6	No. No, I think because there's not any alternatives, right? It's sort of like what do you do with somebody who's got a personality disorder, has impulsivity, has addictions, has anger management problems, and you don't want to put them on a benzodiazepine, right? Like there's not a lot of other options. (Male, full-time community, vulnerable populations, 10-14 years in practice)
My patients are fine on low doses	7	They seem to do fine so I'm not very worried about 50 or 100 [milligrams]. I'm embarrassed to admit, I'm not even sure about the relationship between quetiapine and diabetes so if they've had some blood tests, I check and see what their blood sugar is, and obviously take a look at their weight, but I don't routinely check a blood sugar after they've been on it for a while. (Male, fulltime community practice, > 15 years in practice)
Prescribing influences	8	If I were to hazard a guess, it would be, if it's becoming more popular, that it would be just something that you're seeing your colleagues using and you're seeing specialists using so you tend to use it a bit more. (Female, fulltime community, 10-14 years in practice)
	9	I've renewed it in patients who have had it for awhile and they're stable on their medications, I certainly renew it, though when I do, I ask why they're taking the medication and often times they don't really know why they're on it. (Male, fulltime community practice, 5-9 years in practice)
	10	I do tend to just continue. I think the only time that I would necessarily reevaluate, I reevaluate their mood on a regular basis but I think the only time that I would reevaluate their medications is if their mood was not as good as we would like it to be. I've had patients who have been on it a long time and they are counseled by me on the risks of staying on it long-term and they say, doctor, I want it, it helps me sleep and I feel better and my mood is better and I, they accept the risk and they want to stay on it. (Female, community practice, 5-9 years in practice)

Appendix A: Interview Guide

Main Topic Area	Specific Approach
Interview set up	Greeting, safe environment, study overview, purpose, consent and anonymity issues and express thanks.
Lead in (general exploratory question)	Can you tell me a little bit about the number and types of mental health patients you see in your practice?
Focus on prescribing	What are your tendencies when it comes to prescribing medication? If you can, walk me through your thought processes. (*Probe gently, this is a sensitive area*)
Focus on quetiapine	In the last few years, quetiapine, has been used by some family physicians. Have you prescribed quetiapine for any of your patients? Probes: - Can you give me some examples? (e.g. condition, if continuation, initiation) - What has been your experience of using quetiapine? *(ask for details, repeated examples)* In what situations would you consider quetiapine the drug of choice, or alternatively, the drug to avoid in in this patient population? Probes: a. How do you follow up patients on quetiapine…specifics b. Can you describe how you have come to use quetiapine? (influences – probes – patient request, pharma)
Wrap up	Anything you'd like to add? Thank you and end interview

Appendix B: Themes and subthemes describing family physicians use of quetiapine

Main theme		Subtheme		Codes	
1.	Mental health plus	1.1	General use – it takes the edge off	1.1.1	Psychosis
				1.1.2	Depression
				1.1.3	Anxiety
				1.1.4	Behavioural disorders
				1.1.5	Insomnia/sleep disturbances
		1.2	Complex Conditions of Use	1.2.1	Patients who are unresponsive to first line therapy
				1.2.2	Patients with multiple/unclear psychiatric diagnoses or psychological and social complexity
2.	Choose cautiously – the lesser of two evils	2.1	Avoid addictive medication	2.1.1	Avoiding benzodiazepines
				2.2.1	Less harmful than alternatives
3.	My patients are fine on low doses			3.1.1	Use of low dose
				3.1.2	Side-effects
				3.1.3	Monitoring
4.	Prescribing influences			4.1	Learning in general
				4.2	Learning through peers
				4.3	Learning with psychiatrist
				4.4	Pharma not perceived as an influence

Appendix C: Additional sample quotes to illustrate themes and subthemes

IV=interview

Main theme	Subtheme	Additional quotes
1.Mental health plus	1.1 General use – it takes the edge off	Mhm, so to me the most common reason for using quetiapine would be as a sedative…(IV4, L244) So its definitely, it's not kind of my standard approach to somebody with anxiety….. I mean I obviously have a bit of a concern that I'm using it, you know, sort of off-label. I mean it's not been prescribed as a sleep aid. (IV 7, L257-8) …it really helps. I'm not too sure how it works but it does. (IV 11, L772) So I mean most of the reason in any situation that I've used quetiapine has been to like take advantage of the sedative properties, so situations where you kind of want that benefit and possibly, you know, any other, I don't know, people just seem to find it calming. (IV 15, L357-60)
	1.2 Complex Conditions of Use	*1.2.1 Patients who are unresponsive to first line therapy* The niche for me is that patient with depression who still has issues either with some, any depressive symptoms that are lingering… That depressed patient maybe who still ruminates a lot at night and, therefore, they have a hard time going to sleep and it's related to kind of their mind not shutting down, and I've seen it work quite nicely for that. (IV 9, L 142-147) So I usually start with an antidepressant and if there is, if there's still a fair bit of anxiety or agitation or sleep disturbance, that's when I will often add quetiapine. (IV 10, L88-90) *1.2.2 Patients with multiple/unclear psychiatric diagnoses or psychological and social complexity*

		Yeah, then I got the borderline personality sometimes. They don't react to the simple SSRIs so I mix them with a low dose of quetiapine. (IV 11, L320-21)
2. Choosing cautiously, the lesser of two evils	Need to avoid addictive medications	Okay, I don't want an addictive medication, I don't want to get them on a Z-drug, I don't think the trazodone is going to, to get to the dose I would need, I don't think it's really what they're after. What else is not addictive that might be kind of conking them out a little bit and maybe have the side effect of helping with their anxiety and that's where I come to quetiapine. (IV 14, L234-237)
3.My patients seem fine on low doses	3.1 Low doses are OK	I certainly have some concerns but at small doses, and I guess I don't know that this is technically correct, but I think of it as being at small doses, the most common concerns with quetiapineare quite mitigated, so like, you know, the weight gain, the metabolic syndrome, diabetes would all be, I think not as significant on the small doses. (IV 13, L258-266) Ah yes, oh, oh yeah, totally forgot about that whole side of things. Yes, we do worry about weight gain and diabetes and all of that stuff with quetiapine but that's more for the patients that are on the higher doses, like if they're on 12.5, not as worried. (IV 2, L565-568)
	3.2 Monitoring	I don't think I have a set schedule, it might depend on age, other risk factors, availability, what else? And how much they're on, so I mean if the patient is on a low dose, I'll probably be aware, okay, when did I last check? Okay, a couple of years ago, that's fine. Um, somebody who maybe has a lot of, who I know has got some risk factors and maybe they're on a high dose of it and they're going to be on it for the foreseeable future because they have a chronic illness that's not getting better, they might need to be screened annually and checked regularly that way. (IV 8, L269-275) Okay, so I've never gone into very higher doses, so the dose that I typically use is 25-50 mg at night. I will tell patients that it can be quite sedating but that's okay, taking it in the evening. The other, I usually won't titrate it up. I think I will just start at 25 and then go to 50, not any kind of slow titration. I will advise patients that it can, and I must admit I can't remember off the top of my head whether at that dose it can but

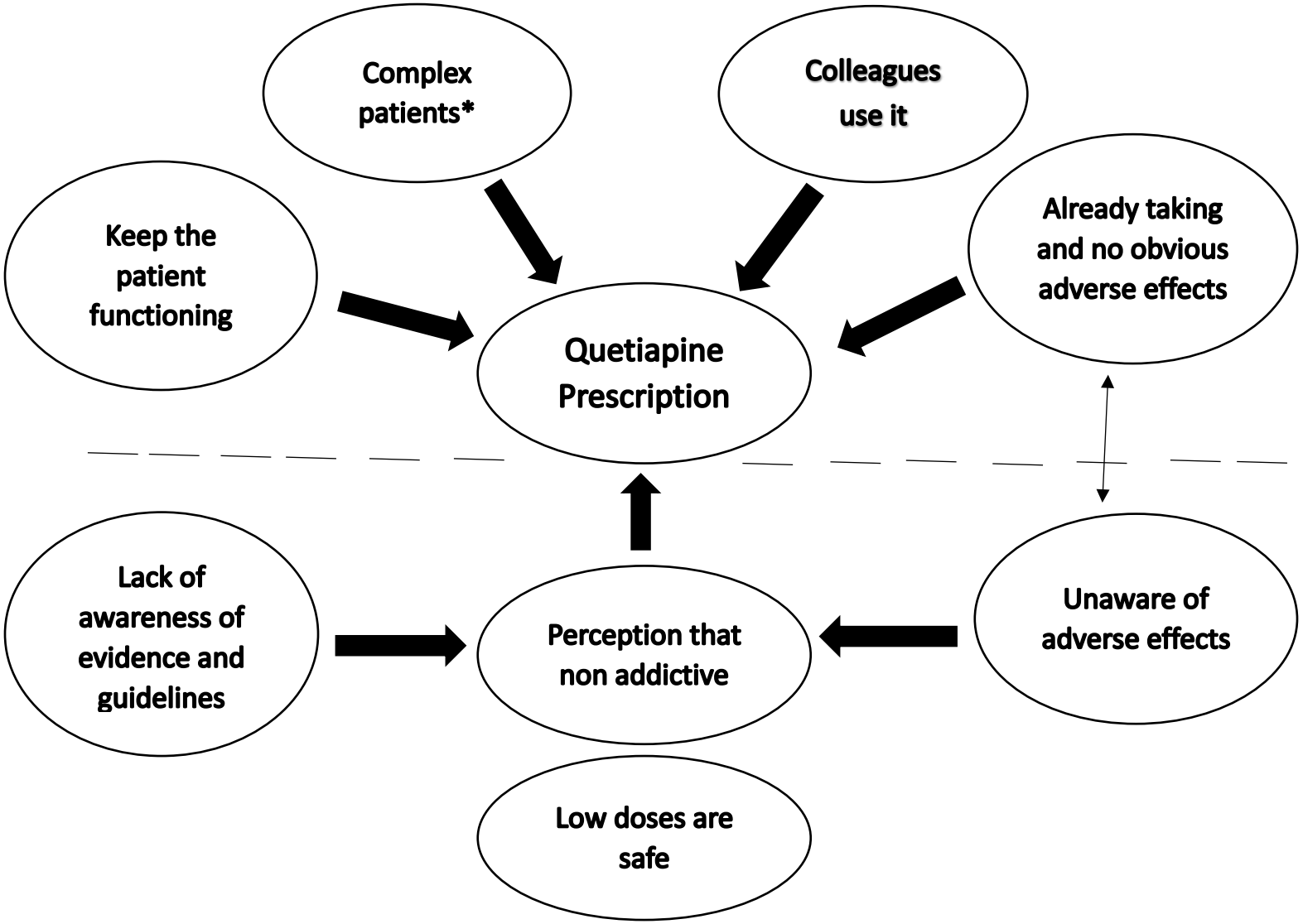
		it can have metabolic effects on things like weight, lipids and glucose. (IV 9, L 106-110) Uh, so I don't routinely like monitor in terms of, you know, like CBC every 3 months, looking to see if their white count is down, something, I don't but I guess I do give it a thought and again, more in, if I see people who are like on higher doses of it, and I don't see actually that many of those people, but I would be doing things like checking their cholesterol or like making sure it's been checked and same with like diabetes screening but I don't have like a hard and fast, you know, like every 3 months. I mean that would be overkill for those things and yeah, I don't do regular like, yeah like liver, like ALT monitoring or anything like that. (IV 13, L 323-329) No, you know, when I was in the hospital, I would do ECGs and I suppose that if somebody would be on a bigger dose of quetiapine, I would, you know, definitely probably do an ECG every year or something like that. If there was a big dose change, I would consider that but honestly, I haven't seen many people recently to think about but yeah, I would probably do, again, the metabolic stuff, you know, cholesterol and liver if somebody was on it for a long time. (IV 6, L 393-396) And I think if I were using larger doses, the few that I've used it in tend to be younger people and people who I'm not concerned about metabolic effects, at least for the short term. I think I would monitor things like weight and lipids and glucose if they were somebody who had issues with those problems. (IV 9, L 127-9)
4.Prescribing influences	Role models (psychiatrists and peers)	I don't actually know how I ended up prescribing quetiapine. Like I really don't remember going to an in-service on this is a great thing to add or, it kind of slipped in and I think it was, I think I was grasping at straws and not sure what else to try and I figured, okay, this patient population is probably a pretty safe thing to try, it's a pretty safe thing to stop, um, just give it a go and I think that, in my case, that's how I ended up doing it. (IV 14, L473-477) I think it does, I mean because there's a lot of, you know, when you get a patient like mine sent back from the specialist on this, there's definitely an impulse just to continue that treatment unless there's clearly a problem with it. If you see that

		happening repeatedly, there may be an increasing drive to, especially if you've had a message that this medicine works for this and you see that the specialists are doing it, that's certainly reinforcing a tendency to actually do that prescription. (IV 8, L 352-356) Um, so prescribing is, I would say, informed by clinical practice guidelines in addition to any CME, be it through journals or conferences but more so by practice of peers and practice of specialists, so again because of my mix of clinical work both in the hospital and within a primary care clinic that has access to specialists who also provide consultation in house, it's through those interactions, you know, with the inpatient psychiatrists as well as the consulting psychiatrists in our community practice that color or inform how I prescribe. (IV 5, L 26-31) Because we're taught that. We're taught that by the psychiatrists. Add a little quetiapine, add a little, you know, before it was the T3, you know, it's like yeah, yeah, but now it's add a little quetiapine. (IV 1, L 553-556) Usually psychiatrists in quetiapine's case, so you just get lots of consults back where they're using quetiapine for various reasons in people who aren't psychotic which, I mean in my view, would be sort of that sort of, was its primary indication when it came out, I think the depression and the bipolar are sort of secondary. (IV 7, L 341-345) In my residency program when we did our psychiatry, the psychiatrists were using it a fair amount and so it's just, you kind of got familiar with it and with quetiapine, especially like it, I don't know, for some reason I was always less scared about it than like risperidone or the other atypical antipsychotics and we were kind of taught, you know, olanzapine causes a ton of metabolic issues but low doses of quetiapine, again, I don't know if this is correct but might not have the same effect so. (IV 15, L 653-658)
	Initiating versus continuing quetiapine prescriptions	She was being treated by a psychiatrist who has now transferred the care back to me but without me having, I sort of see the patient before getting any information from the psychiatrist and they're on a prescription for, among other things, quetiapine, so then I'm stuck in that position of okay, do I continue this medication? I haven't had a

		chance to really assess this patient. They report, oh yeah, I'm doing much better than I was. How much of that is due to that, and that particular patient was actually quite young as well so she's actually probably younger than the quetiapine has an official indication for any kind of antidepressant effect. She's still a teenager where there's sort of warnings about, so she's now on an SSRI and an antipsychotic, and a benzodiazepine and kind of leaves me, you know, sort of pressured to continue all of those medications but I actually still haven't got, I have received an initial assessment from the psychiatrist. I haven't received any note where they've actually started those medicines and have agreed that yes, I think that this would be a good thing to be continuing on them and then I haven't gotten their final note where they say, I think I can stop seeing this person and transfer their care, so, um. (IV 8, L 140-152) There are some patients that I inherit that are on it and our first step is to get them off of it, but you ask them how they got on it and why are they using it and mostly it's their family doc started them on it and why are they using it? Well they think it's the sleep but mostly they really don't know. It's for nerves or to sleep, so you say, well, you know, I think there's other things we can do and let's try these other things and they don't seem to miss it. (IV 3, L 117-124) Um, I think I would probably leave them on them. I don't think I would change them off of that. I don't, yeah, usually most of my patients are coming, you know, from a psychiatrist. If they were coming from sort of another family physician and they were on quetiapine, I would probably leave them on it but I would usually sort of look to see who initiated it and if there was sort of say like a reasonable indication for it. (IV 7, L 531-535) I do tend to just continue. I think the only time that I would necessarily reevaluate, I reevaluate their mood on a regular basis but I think the only time that I would reevaluate their medications is if their mood was not as good as we would like it to be. (IV 2, L 396-398) I've had patients who have been on it a long time and they are counseled by me on the risks of staying on it long-term and they say, doctor, I want it, it helps me sleep

		and I feel better and my mood is better and I, they accept the risk and they want to stay on it. (IV 2, L 133-136) I've renewed it in patients who have had it for awhile and they're stable on their medications, I certainly renew it, though when I do, I ask why they're taking the medication and often times they don't really know why they're on it, and if somebody is taking it purely as a sleep aid where they don't have sort of, again, an axis I disorder, then I question whether we should continue it or not. (IV 6, L 124-127) Also depends on the patient's comfort because when they suffer so significantly from mood disorders, there is a significant reluctance to playing with psychotropic medications when they feel like they've made some progress and stabilize. (IV 5, L 250-252)

Figure 1. Influences that promote off-label use of quetiapine



*Complex patients have incomplete symptom resolution on a single agent, have multiple mental health diagnosis and may also live in unstable environments